

protein is cleaved from the propeptide and it is the active part of the protein. This is described in the present specification (e.g., page 2, third paragraph of the description). It can also be seen in the specification that the sequence descriptions on pages 4 and 5 disclose that the mature human MP121 preferably starts at amino acid 237 of SEQ ID NO. 2 and/or that the mature mouse MP121 also preferably starts at amino acid 237 of SEQ ID NO. 4. It is submitted that if the active sections of both proteins are aligned, a high conformity between the two sequences is shown, since 109 of 116 amino acids are identical, and the amino acid sequences deviate at only 7 positions. This corresponds to an identity of 94%. However, based on the fact that some amino acids are similar in chemical terms, and based on the teachings of a widely accepted article on the similarity and changeability of amino acids in proteins, as a basis, (Dayhoff, Atlas of Protein Sequence and Structure, Vol. 5, Supplement 3, 1978 (copy attached)), an actual similarity of 97% between the two sequences is shown.

Further, it is also submitted that the three-dimensional structure of active TGF- $\beta$  superfamily members is greatly determined by intra and intermolecular cystein cross-links. The 9 cysteins in both mature proteins are located at the same positions with identical distances from each other. Given a high amino acid conformity in the active part of the MP121 proteins, the person skilled in the art would understand that the two proteins have similar structures and similar functions. Due to the high similarities between the two proteins, it is submitted that the Examiner's search will reveal comparable references for both proteins, as the search will not only be directed to identical sequences but also to those sequences with slight deviations. Therefore, it is

submitted that searching the two sequences will not pose an undue additional effort for the Examiner.

Additionally, it is noted that in Application No. 09/218,176 which issued into U.S. Patent No. 6,171,584 (from which the present case is a divisional application), Examiner Mertz (the Examiner of this case) was willing to search a method claim involving both MP121 proteins (human and mouse). Therefore, it is submitted that the Restriction Requirement is also contrary to previous decisions of the Patent Office and the Examiner.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300 referencing Attorney Docket Number 100564-00030.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referring to client-matter number 100564-00030.

Respectfully submitted,



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Attachments:        Reference